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Application of: Xu et al.

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Application No.: 09/763,334

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Filed: August 6, 2001

Examiner: Chen, Shin-Lin

For: TREATMENT AND PREVENTION OF  
CANCER AND PITUITARY  
DISORDERS WITH LATS PROTEINS,  
DERIVATIVES AND FRAGMENTS,  
AND LATS KNOCK-OUT ANIMAL  
MODELS

Attorney Docket No.: 6523-020

**INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. §1.56 AND §1.97**

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Sir:

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Applicants respectfully request that the Examiner review the foregoing references and that the references be made of record in the file history of the application.

Since this Information Disclosure Statement is being filed before the mailing of a first Office Action on the merits, Applicants believe that no fee is due in connection with its filing. However, should the Patent Office determine otherwise, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

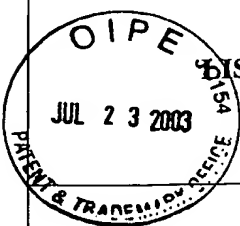
Respectfully submitted,

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Enclosures



# **LIST OF REFERENCES CITED BY APPLICANT**

(Use several sheets if necessary)

ATTORNEY DOCKET NO 6523-020-999	APPLICATION NO. 09/763,334
APPLICANT Xu et al.	
FILING DATE August 6, 2001	GROUP 1646

## **U.S. PATENT DOCUMENTS**

*EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
A	AA 08/939,106		Xu et al.			11/26/97
AB	09/442,102		Xu et al.			11/17/99
AC	60/096,996		Xu et al.			8/18/98
AD	60/096,997		Xu et al.			
AE	5,001,225	3/19/91	Taylor, DW			
AF	5,573,924	11/12/96	Beckmann et al.			
AG	5,994,503	11/30/99	Xu et al.			
AH	6,054,633	4/25/00	Tischfield et al.			
AI	6,359,193	3/19/02	Xu et al.			

## **FOREIGN PATENT DOCUMENTS**

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
						YES NO
AJ	WO 00/10602	03/02/00	PCT			
AK	WO 99/37787	07/29/99	PCT			
AL	WO 96/30402	10/03/96	PCT			
AM	WO 95/31722	11/23/95	PCT			
AN	WO 92/19625	11/92	PCT			
AO	WO 92/10571	6/92	PCT			
AP	EP 0 169 672	1/29/86	EPC			

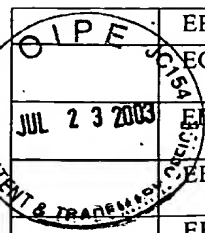
## **OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)**

AQ	Ackermann R. 1988, Monoclonal antibodies. Hum Cell., 1(1):46-53
AR	Bampton et al., 1999, Electrophysiological characterisation of the dentate gyrus in five inbred strains of mouse. Brain Res. 841(1-2):123-34.
AS	Ben-Bassat et al., 2000, Inhibitors of tyrosine kinases in the treatment of psoriasis. Curr Pharm Des. 6(9):933-42. Review
AT	Betz et al., 1996, Bypass of lethality with mosaic mice generated by Cre-loxP-mediated recombination. Curr Biol. 6(10):1307-16
AU	Bier et al., 1989, Searching for pattern and mutation in the <i>Drosophila</i> genome with a P-lacZ vector, Genes Dev. 3:1273-1287
AV	Bishop, 1991, Molecular themes in oncogenesis, Cell 64:235-248
AW	Boedigheimer et al., 1993, Expanded, a negative regulator of cell proliferation in <i>Drosophila</i> , shows homology to the NF2 tumor suppressor, Mechan. Dev. 44:83-84
AX	Boedigheimer and Laughton, 1993, Expanded: a gene involved in the control of cell proliferation in imaginal discs, Development 118:1291-1301
AY	Bowie et al. 1990, Deciphering the message in protein sequences: tolerance to amino acid substitutions. Science. 247(4948):1306-10.
AZ	Brook et al., 1992, Molecular basis of myotonic dystrophy: expansion of a trinucleotide (CTG) repeat at the 3' end of a transcript encoding a protein kinase family member, Cell 68:799-808
BA	Bryant, 1987, Experimental and genetic analysis of growth and cell proliferation in <i>Drosophila</i> imaginal discs, in <i>Genetic Regulation of Development</i> , A.R. Liss, NY, pp. 339-372
BB	Bryant, 1993, Towards the cellular functions of tumor suppressors, Trends Cell. Biol. 3:31-35

BC	Burgess et al. 1990, Possible dissociation of the heparin-binding and mitogenic activities of heparin-binding (acidic fibroblast) growth factor-1 from its receptor-binding activities by site-directed mutagenesis of a single lysine residue. <i>J Cell Biol.</i> 111(5 Pt 1):2129-38
BD	Capecchi, 1989, Altering the genome by homologous recombination, <i>Science</i> 244:1288-1292
BE	Curti BD., 1993, Physical barriers to drug delivery in tumors. <i>Crit Rev Oncol Hematol.</i> 14(1):29-39. Review
BF	DePlaen et al., 1994, Structure, chromosomal localization, and expression of 12 genes of the MAGE family. <i>Immunogenetics.</i> 1994;40(5):360-9
BG	Dietrich et al., 2000, Conditional mutagenesis in mice with heat shock promoter-driven cre transgenes. <i>Mamm Genome.</i> 11(3):196-205.
BH	Dorrington et al. 1965, Immunological studies on the long-acting thyroid stimulator. <i>Clinical Science</i> , 28:165-174
BI	Dymecki et al., 1998, Using Flp-recombinase to characterize expansion of Wnt1-expressing neural progenitors in the mouse. <i>Dev Biol.</i> 201(1):57-65
BJ	Ebert et al., 1988, A Moloney MLV-rat somatotropin fusion gene produces biologically active somatotropin in a transgenic pig. <i>Mol Endocrinol.</i> 2(3):277-83
BK	Fearon and Vogelstein, 1990, A genetic model for colorectal tumorigenesis, <i>Cell</i> 61:759-767
BL	Featherstone and Russell, 1991, Fission yeast p107 <sup>wee1</sup> mitotic inhibitor is a tyrosine/serine kinase, <i>Nature</i> 349:808-811
BM	Fiering et al., 1993, An in-out strategy using gene targeting and FLP recombinase for the functional dissection of complex DNA regulatory elements: analysis of the $\beta$ -globin locus control region, <i>Proc. Natl. Acad. Sci. USA</i> 90:8469-8473
BN	Fortini et al., 1991, The <i>Drosophila zfh-1</i> and <i>zfh-2</i> genes encode novel proteins containing both zinc-finger and homeodomain motifs, <i>Mechan. Dev.</i> 34:113-122
BO	Fu et al., 1993, Decreased expression of myotonic-protein kinase messenger RNA and protein in adult form of myotonic dystrophy, <i>Science</i> 260:235-238
BP	Galsworthy, 1966, Biochemical aspects of temperature sensitivity in neurospora, <i>Diss. Abstr.</i> 26:6348
BQ	Gateff and Mechler, 1989, Tumor-suppressor genes of <i>Drosophila melanogaster</i> , <i>CRC Crit. Rev. Oncogen</i> 1:221-245
BR	Gateff, 1978, Malignant neoplasms of genetic origin in <i>Drosophila melanogaster</i> , <i>Science</i> 200:1448-1459
BS	Gibco BRL Catalogue and Reference Guide, 1992, pp.296
BT	Golic, 1991, Site-specific recombination between homologous chromosomes in <i>Drosophila</i> , <i>Science</i> 252:958-961
BU	Golic and Lindquist, 1989, The FLP recombinase of yeast catalyzes site-specific recombination in the <i>Drosophila</i> genome, <i>Cell</i> 59:499-509
BV	Gura T., 1997, Systems for identifying new drugs are often faulty. <i>Science.</i> 278(5340):1041-2
BW	Hammer et al., 1990, Spontaneous inflammatory disease in transgenic rats expressing HLA-B27 and human beta 2m: an animal model of HLA-B27-associated human disorders. <i>Cell.</i> 63(5):1099-112
BX	Hanks et al., 1988, The protein kinase family: conserved features and deduced phylogeny of the catalytic domains, <i>Science</i> 241:42-52
BY	Hartl et al., 1994, Genome structure and evolution in <i>Drosophila</i> : applications of the framework P1 map, <i>Proc. Natl. Acad. Sci. USA</i> 91:6824-6829
BZ	Hopp T.P. & Woods K.R., 1981, Prediction of protein antigenic determinants from amino acid sequences, <i>Immunol.</i> 78(6):3824-3828
CA	Houdebine LM., 1994, Production of pharmaceutical proteins from transgenic animals. <i>J Biotechnol.</i> 34(3):269-87. Review
CB	Hubbard K. & Ozer H.L., 1995, Senescence and immortalization of human cells, in <i>Cell Growth and Apoptosis</i> ed. Studzinski G.P, ch.12, pp229-249
CC	Hubbard-Smith et al., 1992, Altered chromosome 6 in immortal human fibroblasts, <i>Mol. &amp; Cell. Biol.</i> 12(5):2273-2281
CD	Jacob et al., 1987, Structure of the <i>I(2)gl</i> gene of <i>Drosophila</i> and delimitation of its tumor suppressor domain, <i>Cell</i> 50:215-225
CE	Jain RK., 1994, Barriers to drug delivery in solid tumors. <i>Sci Am.</i> 271(1):58-65. Review
CF	Johnston et al., 1990, The product of the <i>Saccharomyces cerevisiae</i> cell cycle gene <i>DBF2</i> has homology with protein kinases and is periodically expressed in the cell cycle, <i>Mol. Cell. Biol.</i> 10(4):1358-1366
CG	Johnston and Thomas, 1982, The isolation of new DNA synthesis mutants in the yeast <i>Saccharomyces cerevisiae</i> , <i>Mol. Gen. Genet.</i> 186:439-444
CH	Justice MJ., 2000, Capitalizing on large-scale mouse mutagenesis screens. <i>Nat Rev Genet.</i> 1(2):109-15. Review
CI	Justice et al., 1995, The <i>drosophila</i> tumor suppressor gene <i>warts</i> encodes a homologue of human myotonic dystrophy kinase and is required for control of cell shape and proliferation, <i>Genes Dev.</i> 9:534-546
CJ	Kappel et al., 1992, Regulating gene expression in transgenic animals. <i>Curr Opin Biotechnol.</i> 3(5):548-53. Review
CK	Karpen and Spradling, 1992, Analysis of subtelomeric heterochromatin in the <i>Drosophila</i> minichromosome <i>Dp1187</i> by single P element insertional mutagenesis, <i>Genetics</i> 132:737-753
CL	Kennell DE., 1971, Principles and practices of nucleic acid hybridization. <i>Prog Nucleic Acid Res Mol Biol.</i> 11:259-301. Review
CM	Knudson, 1971, Mutation and cancer: statistical study of retinoblastoma, <i>Proc. Natl. Acad. Sci. USA</i> 68(4):820-823
CN	Lai et al., 1993, Loss of function of the <i>Drosophila zfh-1</i> gene results in abnormal development of mesodermally derived tissues, <i>Proc. Natl. Acad. Sci. USA</i> 90:4122-4126
CO	Lützelshwab et al., 1987, A protein product of the <i>Drosophila</i> recessive tumor gene, <i>l(2) giant gl</i> , potentially has cell adhesion properties, <i>EMBO J.</i> 6(6):1791-1797
CP	Mahadevan et al., 1993, Structure and genomic sequence of the myotonic dystrophy (DM kinase) gene, <i>Hum. Mol.</i>



	Genet. 2(3):299-304
CR	Mahoney et al., 1991, The <i>fat</i> tumor suppressor gene in <i>Drosophila</i> encodes a novel member of the cadherin gene superfamily, Cell 67:853-868
CS	Mansfield et al., 1994, Genetic and molecular analysis of <i>hyperplastic discs</i> , a gene whose product is required for regulation of cell proliferation in <i>Drosophila melanogaster</i> imaginal discs and germ cells, Dev. Biol. 165:507-526
CT	McCormick, 1994, Activators and effectors of <i>ras</i> p21 proteins, Current Opinion in Genetics & Development 4:71-76.
CU	McDonald JD., 1995, Using high-efficiency mouse germline mutagenesis to investigate complex biological phenomena: genetic diseases, behavior, and development. Proc Soc Exp Biol Med. 209(4):303-8. Review
CV	Medema et al., 1993, The role of p21ras in receptor tyrosine kinase signaling, Critical Reviews in Oncogenesis 4(6):615-61.
CW	Mitchell and Mitchell, 1954, A partial map of linkage group D in <i>neurospora crassa</i> , Proc. Natl. Acad. Sci. USA 40:436-440
CX	Moreadith et al., 1997 Gene targeting in embryonic stem cells: the new physiology and metabolism. J Mol Med. 75(3):208-16. Review
CY	Mullins et al., 1996, Perspectives Series: Molecular medicine in genetically engineered animals. Transgenesis in the rat and larger mammals. J. Clin. Invest. 98:S37-S40.
CZ	Mullins et al., 1990, Fulminant hypertension in transgenic rats harbouring the mouse Ren-2 gene. Nature. 344(6266):541-4
DA	Mullins et al., 1989, Expression of the DBA/2J Ren-2 gene in the adrenal gland of transgenic mice. EMBO J. 8(13):4065-72
DB	Ollmann et al., 2000, <i>Drosophila p53</i> is a structural and functional homolog of the tumor suppressor <i>p53</i> , Cell 101(1):91-101
DC	Ponder, 1990, Inherited predisposition to cancer, Trends Genet. 6(7):213-218
DD	Ren et al., 1993, Identification of a ten-amino acid proline-rich SH3 binding site, Science 259:1157-1161
DE	Robertson et al., 1988, A stable genomic source of <i>P</i> element transposase in <i>Drosophila melanogaster</i> , Genetics 118:461-470
DF	Rooke et al., 1994, Molecular and genetic characterization of a novel gene which plays an essential role during bristle and photoreceptor development, EMBL Intl. Conf. on <i>Drosophila</i> Development, Crete, Greece, June 19-25, 1994
DG	Rudinger J., 1976, Characteristics of the amino acids as components of a peptide hormone sequence, In Peptide Hormones, ed. J.A Parsons, University Park Press, Baltimore pp1-7
DH	Russell and Nurse, 1987, Negative regulation of mitosis by <i>wee1</i> <sup>+</sup> , a gene encoding a protein kinase homolog, Cell 49:559-567
DI	Sanders P.G., 1990, Protein production by genetically engineered mammalian cell lines, Animal Cell Biotech. 4:15-70
DJ	Sanger et al., 1977, DNA sequencing with chain-terminating inhibitors, Proc. Natl. Acad. Sci. USA 74(12):5463-5467
DK	Sauer and Henderson, 1988, Site-specific DNA recombination in mammalian cells by the Cre recombinase of bacteriophage P1, Proc. Natl. Acad. Sci. USA 85:5166-5170
DL	Schon MP., 1999, Animal models of psoriasis - what can we learn from them? J Invest Dermatol. 112(4):405-10. Review.
DM	Seamark RF., 1994, Progress and emerging problems in livestock transgenesis: a summary perspective. Reprod Fertil Dev. 6(5):653-7. Review
DN	Shortridge et al., 1991, A <i>Drosophila</i> phospholipase C gene that is expressed in the central nervous system, J. Biol. Chem. 266(19):12474-12480
DO	Sigmund CD., 2000, Viewpoint: are studies in genetically altered mice out of control? Arterioscler Thromb Vasc Biol. (6):1425-9. Review
DP	St. John et al., 1999, Mice deficient of <i>Lats1</i> develop soft-tissue sarcomas, ovarian tumors and pituitary dysfunction, Nature Genetics 21:182-86
DQ	Stewart and Denell, 1993, Mutations in the <i>Drosophila</i> gene encoding ribosomal protein S6 cause tissue overgrowth, Mol. Cell. Biol. 13:2524-2535
DR	Strojek et al., 1988, Genetic engineering: Principles and Methods. The use of transgenic animal techniques for livestock improvement. Plenum Press, Vol. 10, pp. 221-246
DS	Tao et al., 1994, Facilitating genetic analysis in mammalian systems using the FLP/FRT recombination system, EMBL Intl. Conf. on <i>Drosophila</i> Development, Crete, Greece, June 19-25, 1994
DT	Tao et al., 1999, Human homologue of the <i>Drosophila melanogaster lats</i> tumour suppressor modulates CDC2 activity, Nature Genetics, 21:177-81
DU	Taurog et al., 1988, HLA-B27 in inbred and non-inbred transgenic mice. Cell surface expression and recognition as an alloantigen in the absence of human beta 2-microglobulin. J Immunol. 141(11):4020-3
DV	Thummel and Pirrotta, 1992, New pCaSpeR P element vectors, Dros. Inf. Svc. 71:150
DW	Tomlinson and Ready, 1987, Cell fate in the <i>Drosophila</i> ommatidium, Dev. Biol. 123:264-275
DX	Török et al., 1993, <i>P-lacW</i> insertional mutagenesis on the second chromosome of <i>Drosophila melanogaster</i> : isolation of lethals with different overgrowth phenotypes, Genetics 135:71-80
DY	Toyn and Johnston, 1994, The Dbf2 and Dbf20 protein kinases of budding yeast are activated after the metaphase to anaphase cell cycle transition, EMBO J. 13(5):1103-1113
DZ	Toyn et al., 1991, The cell-cycle-regulated budding yeast gene <i>DBF2</i> , encoding a putative protein kinase, has a homologue that is not under cell-cycle control, Gene 104:63-70
EA	Vitetta et al., 1994, Monoclonal antibodies as agonists: an expanded role for their use in cancer therapy. Cancer Res. 54(20):5301-9. Review.
	Vogelstein and Kinzler, 1993, The multistep nature of cancer, Trends Genet. 9:138-141

	EB	Wall, RJ., 1996, Transgenic Livestock: Progress and prospects for the future. <i>Theriogenology</i> 45:57-68
	EC	Wang et al., 1994, Identification and characterization of tumor suppressor genes in <i>Drosophila</i> , EMBL Intl. Conf. on <i>Drosophila</i> Development, Crete, Greece, June 19-25, 1994
	ED	Watson et al., 1994, <i>Drosophila</i> in cancer research: the first fifty tumor suppressor genes. <i>J Cell Sci Suppl.</i> 18:19-33. Review
	EE	Watson et al., 1992, <i>Drosophila</i> homolog of the human S6 ribosomal protein is required for tumor suppression in the hematopoietic system, <i>Proc. Natl. Acad. Sci. USA</i> 89:11302-11306
	EF	Weinberg, 1991, Tumor suppressor genes, <i>Science</i> 254:1138-1146
	EG	Wharton et al., 1985, <i>opa</i> : a novel family of transcribed repeats shared by the <i>Notch</i> locus and other developmentally regulated Loci in <i>D. melanogaster</i> , <i>Cell</i> 40:55-62
	EH	Woods and Bryant, 1993, ZO-1, DlgA and PSD-95/SAP90: homologous proteins in tight, septate and synaptic cell junctions, <i>Mechan. Dev.</i> 44:85-89
	EI	Woods and Bryant, 1991, The discs-large tumor suppressor gene of <i>Drosophila</i> encodes a guanylate kinase homolog localized at septate junctions, <i>Cell</i> 66:451-464
	EJ	Woods and Bryant, 1989, Molecular cloning of the <i>lethal(1)Discs large-1</i> oncogene of <i>Drosophila</i> , <i>Dev. Biol.</i> 134:222-235
	EK	Xu and Rubin, 1993, Analysis of genetic mosaics in developing and adult <i>Drosophila</i> tissues, <i>Development</i> 117:1223-1237
	EL	Xu et al., 1995, Identifying tumor suppressors in genetic mosaics: the <i>Drosophila lats</i> gene encodes a putative protein kinase, <i>Dev.</i> 121:1053-1063
	EM	Xu and Harrison, 1994, Mosaic analysis using FLP recombinase, <i>Meth. Cell Biol.</i> 44:655-682
	EN	Xu and Artavanis-Tsakonas, 1990, <i>deltex</i> , a locus interacting with the neurogenic genes, <i>Notch</i> , <i>Delta</i> and <i>mastermind</i> in <i>Drosophila melanogaster</i> , <i>Genetics</i> 126:665-677
	EO	Yang et al. 2001, Human homologue of <i>Drosophila lats</i> , LATS1, negatively regulate growth by inducing G(2)/M arrest or apoptosis. <i>Oncogene</i> . 20(45):6516-23
	EP	Yarden et al., 1992, <i>cot-1</i> , a gene required for hyphal elongation in <i>Neurospora crassa</i> , encodes a protein kinase, <i>EMBO J.</i> 11(6):2159-2166
	EQ	Yavari et al., 1994, Isolation of genes whose expression is regulated by the <i>Drosophila</i> mutant tumor suppressor gene <i>lats</i> , EMBL Intl. Conf. on <i>Drosophila</i> Development, Crete, Greece, June 19-25, 1994

EXAMINER

DATE CONSIDERED

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